REMARKS

Claims 1-39 are pending in the application. Claims 18-39 were previously withdrawn from consideration. Applicants file herewith under 35 U.S.C. § 1.132 the Declaration of Marlene Darfler, a co-inventor of the present application.

Applicants note with appreciation that the Examiner has withdrawn all rejections other than those discussed below.

Rejections Under 35 U.S.C. §102

Wang et al.

Claims 1-17 are rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,672,696 by Wang et al. ("Wang") from the IDS dated 29 May 2007. The Examiner states that "Wang et al. teach a method of treating paraffinized tissue samples to release analytes." (Office Action at page 2). The Examiner further states that "[a]lthough Wang et al. intended to analyze DNA, and *subsequently* discard the supernatant, the method they teach recites every step instantly claimed in claims 1-17." (Office Action at page 3; emphasis in original). The Examiner therefore concludes that Wang anticipates claims 1-17. Applicants respectfully disagree.

Claim 1 as pending is directed towards a method of preparing a biomolecule lysate and requires two steps:

(a) heating a composition comprising a histopathologically processed biological sample and a reaction buffer at a temperature and a time sufficient to reverse or release protein cross-linking in said biological sample, and

(b) treating the resulting composition with an effective amount of a proteolytic enzyme for a time sufficient to disrupt the tissue and cellular structure of said biological sample. Claim 1 further requires that the "biomolecule lysate is in a soluble liquid form **suitable for protein expression analysis** and wherein the content of said lysate is **representative of the total protein content** of said histopathologically processed biological sample." (Emphasis added.)

As demonstrated in the attached declaration of Marlene Darfler (the "Darfler Declaration") and the accompanying figures thereto, an experimental regime was performed comparing the methods of the instant application as recited in claim 1 and the methods described by Wang. Ms. Darfler determined that the protocol disclosed by Wang does not result in a

biomolecule lysate in a soluble liquid form suitable for protein expression analysis, and that the biomolecule lysate is not representative of the total protein content, as required by claim 1 of the instant application. (Darfler Declaration at ¶¶ 10, 19 and 24.)

Formalin fixed paraffin embedded mouse liver tissue was used as the starting material in each protocol. (Darfler Declaration at ¶10.) Ms. Darfler indicates that using Expression Pathology's Liquid Tissue MS Protein Prep Kit manual is consistent with the method of claim 1, and results in a biomolecule lysate contained in a single tube that is in a visibly soluble liquid form. (Id.) In contrast, performing the Wang protocol as provided in Example 1 of Wang results in three separate fractions: an insoluble fraction, a visibly soluble fraction, and a DNA fraction rendered visibly soluble after DNA precipitation. (Darfler Declaration at ¶11.) The Liquid Tissue lysate and the two visibly soluble fractions from the Wang protocol were subjected to mass spectrometric (MS) analysis, which is capable of identifying thousands of individual peptides and proteins in a single analysis and thereby providing an overall representation of protein expression in a biomolecule lysate. (Darfler Declaration at ¶13.) The Liquid Tissue protocol identified 1,251 different, unique proteins from a sample of formalin fixed paraffin embedded mouse liver tissue. (Darfler Declaration at ¶15.) In contrast, only 107 different, unique proteins were identified in the liquid fraction resulting from the Wang protocol, and only 12 different, unique proteins were identified in the resuspended DNA fraction from the Wang protocol. (Darfler Declaration at ¶¶ 16-17.)

Ms. Darfler also describes how analyses were performed using the Gene Ontology (GO) program to identify the representation of various sub-cellular locations in a given biomolecule lysate. (Darfler Declaration at ¶20.) While GO analysis of the Liquid Tissue lysate demonstrated the isolation of proteins from 124 different regions across every part of the cellular milieu, GO analysis of the Wang liquid fraction returned only 30 regions, and the proteins resulting from the DNA fraction of Wang were from only 8 different regions. (Id.)

Further, the relative content of proteins involved in liver function was determined among the Liquid Tissue preparation biomolecule lysate and the two fractions resulting from the Wang protocol. (Darfler Declaration at ¶21.) In the Liquid Tissue lysate, a total of 677 proteins of the 1,251 proteins identified are involved in normal liver function, while there were 10 liver function proteins identified in the Wang liquid fraction lysate and 3 in the Wang DNA fraction lysate. (Id.)

Finally, Ms. Darfler notes that in the experimental analyses performed under her direction, the Liquid Tissue lysate contained all four of the standard proteins that are produced by the liver and whose presence is assayed for in the blood in a widely-applied clinical assay: alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate aminotransferase, and albumin. (Darfler Declaration at ¶22.) None of these four proteins were detected in either of the Wang fractions. (Id.)

On the bases of these empirical results, Ms. Darfler concludes that the Liquid Tissue lysate is representative of the starting material originating from a histopathologically processed liver sample. (Darfler Declaration at ¶23.) Furthermore, it is Ms. Darfler's opinion that the lack of liver function proteins identified in the Wang preparations indicates that these lysates are not representative of the total protein content of the starting material originating from a histopathologically processed liver sample. (Darfler Declaration at ¶¶23-24.)

For these reasons, Wang does not teach all the limitations of instant claim 1. Claims 2-17 depend from claim 1 and thus stand or fall with this claim. Thus, Applicants assert that pending claims 1-17 are not anticipated by Wang.

Banerjee et al.

Claims 1-4 and 7-17 stand rejected under 35 U.S.C. § 102(b) as anticipated by Banerjee et al. ("Banerjee")(BioTechniques vol. 18:768-73, 1995). The Examiner states that "Banerjee et al. teach a method of retrieving useful analytes from paraffin-embedded tissue samples." (Office Action at page 3). The Examiner further states that "[i]nherently, because Banerjee describes all the method steps instantly claimed, these teachings must arrive at the instantly claimed invention." (Office Action at page 5). The Examiner therefore concludes that Banerjee anticipates each and every step of the instant claims. Applicants respectfully disagree.

The methods of the instant application as recited in claim 1 were compared to the methods described by Banerjee, and Ms. Darfler determined that the protocol disclosed by Banerjee does not result in a biomolecule lysate in a soluble liquid form suitable for protein expression analysis, and that the biomolecule lysate is not representative of the total protein content, as required by claim 1 of the instant application. (Darfler Declaration at ¶¶ 10, 19 and 24.)

Performing the Banerjee protocol as provided at pages 770-72 of Banerjee results in two separate fractions: an insoluble fraction and a visibly soluble fraction. (Darfler Declaration at ¶12.) The Liquid Tissue lysate and the visibly soluble fraction from the Banerjee protocol were subjected to MS analysis. (Darfler Declaration at ¶13.) As stated above, the Liquid Tissue protocol identified 1,251 different, unique proteins from a sample of formalin fixed paraffin embedded mouse liver tissue. (Darfler Declaration at ¶15.) In contrast, only 15 different, unique proteins were identified in the liquid fraction resulting from the Banerjee protocol. (Darfler Declaration at ¶¶ 15, 18.)

Ms. Darfler also describes how analyses were performed using the Gene Ontology (GO) program to identify the representation of various sub-cellular locations in a given biomolecule lysate. (Darfler Declaration at ¶20.) While GO analysis of the Liquid Tissue lysate demonstrated the isolation of proteins from 126 different regions across every part of the cellular milieu, GO analysis of the Banerjee liquid fraction returned only 8 regions. (Id.) The relative content of proteins involved in liver function was similarly lopsided between the Liquid Tissue preparation biomolecule lysate and the biomolecule lysate from the Banerjee protocol: in the Liquid Tissue lysate, a total of 677 proteins were identified as involved in normal liver function, while only 2 liver function proteins were identified in the Banerjee lysate. (Darfler Declaration at ¶21.)

Moreover, the Liquid Tissue lysate contained all four of the clinically-assayed proteins, while none of these four proteins were detected in the Banerjee biomolecule lysate. (Darfler Declaration at ¶22.)

On the bases of these empirical results, it is Ms. Darfler's opinion that the Banerjee preparation is not representative of the total protein content of the starting material originating from a histopathologically processed liver sample. (Darfler Declaration at ¶24.)

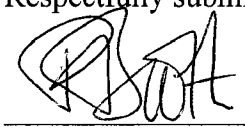
For these reasons, Banerjee does not teach all the limitations of instant claim 1. Claims 2-17 depend from claim 1 and thus stand or fall with this claim. Thus, Applicants assert that pending claims 1-17 are not anticipated by Banerjee.

CONCLUSION

In view of the foregoing amendments and remarks, applicants respectfully submit that the application is in condition for allowance. Should the Examiner feel that there are any issues outstanding after consideration of this response, the Examiner is invited to contact the undersigned to expedite prosecution of the application.

The Commissioner is hereby authorized by this paper to charge any fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-3840. **This paragraph is intended to be a CONSTRUCTIVE PETITION FOR EXTENSION OF TIME in accordance with 37 C.F.R. § 1.136(a)(3).**

Respectfully submitted,



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Paul M. Booth
Attorney for Applicant
Reg. No.: 40,244

Proskauer Rose LLP
1001 Pennsylvania Avenue, NW
Suite 400
Washington, DC 20004
Telephone: 202.416.6800
Facsimile: 202.416.6899
CUSTOMER NO: 61263

Customer No. 61263